Paper No. 33

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte PHILLIP D. COOK,
THOMAS BRUICE,
CHARLES J. GUINOSSO,
ANDREW M. KAWASAKI
and RICHARD GRIFFEY

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Appeal No. 1999-1407
Application No. 08/295,744

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ON BRIEF

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Before WINTERS, ROBINSON and ADAMS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-40 and 59-68, which are all the claims pending in the application.

Claim 1 is illustrative of the subject matter on appeal and is reproduced below:

1. A compound of the structure:

G_0-G_1-G_2-G_3

wherein:

G_0 is a nucleoside, a nucleotide or an oligonucleotide;
G_1 is a bivalent linking moiety;
G_2 is an aryl or heteroaryl moiety; and
G_3 is a nitrogen-containing heterocyclic RNA cleaving chemical functional group having general acid/base properties.

The references relied upon by the examiner are:

Marvin H. Caruthers (Caruthers), Synthesis of Oligonucleotides and Oligonucleotide Analogues, in ANTISENSE INHIBITORS OF GENE EXPRESSION 7-22 (J.S. Cohen ed., CRC press, Boca Raton, FL, 1989)

Mitchell et al. (Mitchell), "Boron trifluoride-methanol complex as a non-depurinating detritylating agent in DNA synthesis," Nucleic Acids Research, Vol. 18, No. 17, p. 5321 (1990)

Bergstrom et al. (Bergstrom), "Organoiron-Mediated Alkylation of Phosphite Esters: Synthesis of (Dicarbonyl)(?^{5}-cyclopentadienyl)iron-Derived Nucleoside Phosphonate Esters," J. Org. Chem., Vol. 57, pp. 873-876 (1992)

Gura, "Antisense Has Growing Pains," Science, Vol. 270, pp. 575-577 (1995)

GROUND OF REJECTION

Claims 1-40 and 59-68 stand rejected under 35 U.S.C. § 112, first paragraph, as being based on an insufficient disclosure to support or enable the scope of the claims currently claimed.

We reverse.

DISCUSSION

In reaching our decision in this appeal, we considered appellants' specification and claims, in addition to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's Answer[1] for the examiner's reasoning in support of the rejection. We further reference appellants' Brief[2], and appellants' Reply Brief[3] for the appellants' arguments in favor of patentability. We note the examiner entered and considered appellants' Reply Brief.[4]

THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

"When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement." In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). "[It] is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for

[1] Paper No. 30, mailed December 10, 1998.
[2] Paper No. 29, received November 9, 1998.
[3] Paper No. 31, received February 12, 1999.

the applicants to go to the trouble and expense of supporting his presumptively accurate disclosure." In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971).

On this record, the examiner finds (Answer, page 4) that appellants' "disclosure is enabling only for claims limited to the compounds whose mode of synthesis has been demonstrated in the specification and whose functionality has been shown." We note that the examiner makes no effort to identify those compounds he considers to be enabled by appellants' disclosure. Instead, the examiner argues (id.) that the "breadth of these claims includes an enormous variety of compounds, the specification lacks guidance on methods of synthesis of each compound and whether the claimed compounds would function in the assay or would inhibit the assay."

With regard to the enabling scope of appellants' disclosure, as it applies to "how to make" the claimed compounds, the examiner argues (Answer, page 4) "[t]here is specific prior art which indicates that the synthesis of new nucleotide analogues is not a trivial process and is prone to failure." To support this conclusion, the examiner relies on three prior art references. The examiner applies Bergstrom (id.) to teach that "attempts to apply the reaction to the synthesis of an oligothymidine analogue failed because Fp ethylene apparently reacts with phosphotriester groups…." However, as appellants point out (Brief, page 7) Bergstrom shows "simply that those skilled in the art were aware of two techniques

[4] Paper No. 32, mailed February 25, 1999.

for preparing certain types of oligonucleotides, … and that the authors were unsuccessful in their attempts to develop yet another [third] technique…." We agree with appellants. Bergstrom teach (page 873):

> Modification at phosphorus can be achieved in conventional phosphoramidite or H-phosphonate synthesis protocols by (1) utilizing modified mononucleoside building blocks or (2) replacing the oxidation cycle with a reaction that yields the modified phorphorus linkage. The first approach works well for the construction of methylphosphonate-linked oligonucleotides, while the second approach is appropriate for phosphoramidate-linked oligonucleotides.
>
> …
>
> One goal of our research is the development of new construction techniques for oligonucleotide analogues substituted at phosphorus by transition metal complexes.

It is Bergstrom's "new construction technique for oligonucleotide analogues" that failed.

The examiner applies Mitchell as another example that synthesis of new nucleotide analogues is prone to failure. According to the examiner (Answer, bridging sentence, pages 4-5) Mitchell "states '[t]he title complex (I) is less convenient than Cl_2CHCO_2H (II) for routine automated DNA synthesis, but it is highly effective in the synthesis of purine-rich oligomers that fail to give adequate yields with II (abstract)'." Initially, we note that the examiner's citation is to a "CAPLUS" abstract, and not to the Mitchell publication. The sentence cited by the examiner is the last sentence of the Mitchell article, which states in full "BTMC is less convenient than DCA for routine synthesis but it is a highly effective non-depurinating detritylating agent in the synthesis of purine-rich oligomers that fail to give adequate yields with DCA." As appellants point out (Brief, page 6) Mitchell "simply states that

the synthesis of certain oligomers fails to 'give adequate yields' with one reagent…." Nevertheless, appellants note that Mitchell "in fact, shows that those skilled in the art seeking higher yields have at their disposal an alternative reagent that is said to be 'highly effective' in the synthesis of such oligomers…." We agree with appellants.

Finally, the examiner relies on Caruthers (Answer, page 5) to teach "[i]f DNA analogues are to be tested as potential therapeutic agents, gram and even kilogram quantities of various analogues must be produced in homogenous form. Clearly the chemistry needed to accomplish this goal is beyond our present capabilities…." To this appellants' argue first (Brief, page 7) that the "reference … states that '[r]ecent advances in DNA chemistry now make it possible for biochemists, molecular biologists and cell biologists to prepare and use synthetic DNA' (page 22, section 8)" [alteration original]. Appellants' then argue (id.) that while Caruthers:

> indicates that it can be difficult to produce oligonucleotide analogs both in kilogram quantities and in homogeneous form …, the reference nowhere so much as suggests that those skilled in the art would not be able to produce such compounds in lesser quantities and/or in a form that is not entirely homogeneous.

We agree with appellants. From this reference, the examiner's concern appears to be the ability to make sufficient quantities of DNA analogues necessary to test "potential therapeutic reagents." The claims, however, are not drawn to "therapeutic reagents," instead, they are drawn to compounds. According to the specification (page 7) the claimed compounds have use in diagnostic applications. As appellants point out (Brief, page 7) Caruthers "nowhere so much as suggests

that those skilled in the art would not be able to produce such compounds in lesser quantities and/or in a form that is not entirely homogeneous" for use as non-therapeutic reagents.

Focusing on the use of the claimed compounds as therapeutic reagents, the examiner finds (Answer, page 8) that Gura "expressly notes that no antisense therapy has yet been shown to function. Such a negative teaching in the art supports the rejection by providing prima facie [sic] evidence of non-enablement." However, as set forth, supra, and argued by appellants (Reply Brief, page 4) "there is no requirement in the claims (or elsewhere) that the compounds be used solely in antisense therapy, or that they function through any particular mechanism." Appellants argue (id.) that "[a]lthough the [e]xaminer contends that it would be difficult to predict whether or not the claimed compounds can be used in antisense therapy, the [e]xaminer fails to explain how this contention, even if true, could possibly demonstrate the absence of a patentable use for the compounds." We agree with appellants, that the use of the claimed compounds is not limited to antisense therapy. The examiner has not addressed the issue of enablement with respect to appellants' other disclosed uses for the claimed compound.

We recognized the examiner's reliance on Morton International Inc. v. Cardinal Chemical Co., 5 F.3d 1464, 1469-70, 28 USPQ2d 1190, 1194 (Fed. Cir. 1993). Specifically, the examiner finds (Answer, page 7) that "the [Morton] court states on page 1194 that, '[o]n review of the record, there is considerable evidence showing that those skilled in the art could not make the claimed compounds using

the procedures of the specification, and no evidence that such compounds even exist…'" As appellants emphasize (Reply Brief, page 3, n. 1) "there was 'considerable evidence' in Morton 'showing that those skilled in the art could not make the claimed compounds." As discussed, supra, there is no such evidence present on this record.

In our opinion, for the reasons set forth above, the examiner failed to present the evidence necessary to meet his burden of proving that the claimed invention is not adequately enabled by the description of the invention provided in appellants' specification. Accordingly, we reverse the rejection of claims 1-40 and 59-68 under 35 U.S.C. § 112, first paragraph.

We recommend the examiner review Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 52 USPQ2d 1129 (Fed. Cir. 1999), since the court provided a model analysis of enablement issues and illustrated the type of fact finding which is needed before one is in a proper position to determine whether a given claim is enabled or non-enabled. In addition, we remind the examiner that in satisfying his burden under 35 U.S.C. § 112, first paragraph, it is impermissible to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such

reference fairly suggests to one skilled in the art. Compare In re Wesslau, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965); In re Mercer, 515 F.2d 1161, 1165-66, 185 USPQ 774, 778 (CCPA 1975).

REVERSED

SHERMAN D. WINTERS	)
Administrative Patent Judge	)
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	) BOARD OF PATENT
DOUGLAS W. ROBINSON	)
Administrative Patent Judge	) APPEALS AND
	)
	) INTERFERENCES
	)
DONALD E. ADAMS	)
Administrative Patent Judge	)

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